The Use of Antabus in the Therapy of Alcoholic Patients

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SUMMARY

Preliminary studies on the effects of antabus (tetraethylthiuram disulfide) in the therapy of alcoholic patients indicate that it is very valuable in providing a "chemical foundation" for sobriety, even in those with a severe, long term drinking problem. In the first 30 patients treated, a favorable degree of control of the alcoholism has been effected in approximately 80 per cent. When taken regularly the drug maintains in the patient a very high degree of sensitivity to alcohol, quickly producing a number of very distressing bodily reactions whenever even very small amounts of spirits are ingested. Because of its potential dangers, antabus should be used only after thorough clinical and laboratory studies in properly staffed institutions. It is contraindicated in individuals with existing major psychosis or drug addiction and must be used only with caution in patients with diabetes mellitus, cardiovascular disease, goiter, pregnancy, epilepsy, asthma, and hepatic disease. Antabus therapy should be considered only one aspect of the total treatment program for the alcoholic patient.

PERHAPS the greatest difficulty in the treatment of the alcoholic patient is that often he will not remain sober long enough to undergo any real therapy. Some authorities have therefore stated that a minimum of six months to one year of hospitalization is required to lay a foundation before allowing the patient to return to his usual environs and continue treatment. Others have used conditioned reflex (aversion) therapy, first with apomorphine and later with emetine, with varying degrees of success; but this method depends on the after-effects of a short period of conditioning.

About two years ago in Denmark two physicians discovered more or less accidentally that tetraethylthiuram disulfide, or antabus, when ingested prior to drinking would chemically sensitize the individual against alcohol.[2] Since then over 10,000 problem drinkers have been treated with this drug in this country and abroad, under pretty carefully controlled conditions for the most part.[1, 3, 4]

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Antabuse® was supplied through the courtesy of Ayerst, McKenna and Harrison, Ltd., New York.

Presented by the Section on Psychiatry and Neurology at the 79th Annual Meeting of the California Medical Association, April 30-May 3, 1950, San Diego.

INDICATIONS

Since in almost every alcoholic a combination of pharmacodynamic and psychodynamic factors is encountered, no single therapeutic approach is usually effective, but instead a comprehensive program is required. However, it can now be stated that the antabus regimen offers a pretty good "insurance policy" for sobriety in the majority of these patients. Therefore, the author has been using it in almost every case except where the alcoholism is relatively mild or is strictly secondary to a well-defined psychiatric disorder that necessitates primary attention. For example, a person using alcohol mostly in reaction to some acute situational stress might not require antabus, at least as a long-term program.

Of course, the interest in antabus on the part of the public as well as physicians has been rather thoroughly aroused. The manufacturers of the drug reportedly have been receiving 500 inquiries a month about it. The idea of overcoming a very expensive, disabling disorder like alcoholism "by taking a few pills" has fired the imagination of many a worried relative as well as that of many unhappy victims of the condition. Unfortunately, a little reflection makes evident that it is not nearly so simple as that, for the use of the drug is only one component of the therapeutic program.

CONTRAINDICATIONS

For the most part, these are relative rather than absolute. Two deaths have been reported in Europe in patients treated with antabus and suffering from diabetes mellitus, but other diabetics have been successfully treated without complications. Since in the alcohol reaction the cardiac rate and the cardiac output increase, the drug must be used cautiously in patients with cardiovascular disease. Opinion varies as to the use of antabus in patients with considerable liver damage, but the author has treated several such patients without incident, although care was taken to employ proper supportive measures of a nutritional and biochemical sort. Pregnancy has been considered a contraindication, although it is reported that a few gravid women have been successfully managed on the program, and at present the author is treating one in about the fifth month.

Perhaps the two most important conditions interfering with antabus therapy are psychiatric in nature—namely, drug addiction and definite psychosis. In the former case, the patient might take more and more of the habituating drug when deprived of alcohol; in the latter, the patient might use antabus for suicide or otherwise misuse the drug.

Asthma, nephritis, goiter, and epilepsy are other conditions which indicate a cautious approach to antabus therapy.

PRELIMINARY STUDIES

First of all, the alcoholic patient must have, of course, careful physical and neuropsychiatric examination. The author also employs comprehensive laboratory and biochemical studies. In addition to routine tests like blood cell count and urinalysis, serum calcium, phosphorus, glucose, cholesterol total and cholesterol esters, iodine, and bicarbonate levels are determined. A battery of tests are used to investigate liver function thoroughly: Cephalin flocculation, thymol turbidity, albumin-globulin ratio, serum alkaline phosphatase, serum bilirubin level, and sulfobromophthalein excretion rate. Blood acetaldehyde is measured before and after alcohol test reactions, since this is the constituent most affected by antabus and the one presumed to be most important in the sensitization mechanism. Electrocardiographic and electroencephalographic studies are carried out.

PROCEDURE

The alcoholic must be detoxified thoroughly and must be completely off alcohol for at least 48 hours prior to starting antabus medication. Usually he then is given three tablets within 24 hours and about 12 hours later two ounces of spirits is given to test the reaction. If the reaction is very slight, it is sometimes advisable to give an additional two ounces of spirits in one hour. Antabus is continued (one 0.5 gm. tablet at bedtime) and two additional reaction tests are ordinarily given at 48-hour intervals, using progressively smaller test doses of alcohol.

In a satisfactory reaction test, the patient usually shows a heavy flush within ten minutes after ingestion of 1 ounce of spirits, followed by heart-pounding, a feeling of constriction in the chest and throat, and often nausea, headache, and dizziness. The odor of acetaldehyde is almost always easily detectable. After one-half to one hour the patient often drops off to sleep.

It is important to emphasize the virtual necessity of the patient's experiencing two to three full-fledged reactions to alcohol under controlled conditions after being sensitized by intake of the drug. For him to learn about the reaction from hearing about it or even from seeing other patients experience it is usually not sufficient; he must actually undergo the process and in that way imprint the effects on the "feeling levels" of his own nervous system. After an adequate, or "Grade III," response, many an alcoholic verbally expresses a heartfelt aversion to spirits that surpasses any effects produced by conditional reflex therapy with emetine. More important than the psychological effect, perhaps, is the alteration in the pharmacodynamic factor, so that the patient often manifests a true indifference to alcohol even after returning to his usual environs.

Once the patient has experienced a satisfactory response, it is frequently feasible for him to return home with a limited supply of antabus and continue on an out-patient basis. He must continue to take the prescribed dose daily, under supervision by a member of his family if possible. So far the only relapses observed have occurred when the patient consciously or unconsciously neglected to take antabus for several days running. Then, since unbeknownst to him some antabus effect still remained, he often has given himself a painful surprise, becoming quite sick for 24 to 48 hours after ingesting several drinks. Usually by that time the patient is more than willing to return to the hospital and get back on the program.

CORRELATED THERAPY

Having given the patient a chemical foundation for abstinence, the other clinical problems that are usually found in the problem drinker must be dealt with. These are covered by psychiatric care as indicated, including group therapy; by nutritional and endocrine rehabilitation; and by appropriate efforts at social readjustment through counseling of the family and of the employer by the physician or psychiatric social worker.[5] It should be stressed that for most alcoholics antabus is not a therapy in itself but rather a valuable gateway to more fundamental treatment.

The need for appropriate psychotherapy along with medication in the case of the majority of problem drinkers has been emphasized by most of the workers in this line of research, including the Danish physicians who pioneered it. In the first place the alcoholic requires guidance and reorientation in his whole life program. Many alcoholics have profound emotional tensions which have been partly masked by alcoholism and which become in some ways even more disturbing when they are on the sobriety program. Although 40 per cent of problem drinkers are estimated to function pretty well through abstinence alone, the remaining 60 per cent show well defined neuroses or other psychopathologic conditions requiring therapy. In the case of the latter group, to supply antabus without correlated psychiatric treatment would be to treat only one symptom and to ignore the basic problems of the individual.

By the same token, the majority of the problem drinkers show a variety of physical ailments associated with alcoholism. In addition to the well-known anatomical disturbances like gross hepatic cirrhosis and polyneuropathy, more subtle nutritional and biochemical deviations are assuming greater and greater importance as techniques of investigation improve.[6] For instance, many patients have low glucose tolerance and a tendency toward hypoglycemia,[7] apparently on the basis of hypofunction of the adrenal cortex. This disturbance of course is associated clinically with symptoms like "jitters," tension, and fatigue—commonly blamed by some individuals for their inability to remain sober. In others unpleasant physical symptoms like tiredness and tension are associated with low blood iodine, high serum calcium, disturbance in the calcium-phosphorus ratio of the serum, and an elevated serum cholesterol—all associated with diminished thyroid function. In many patients, vague gastro-

intestinal complaints are found to be related to milder forms of hepatic dysfunction, reflected in low serum cholesterol, high serum alkaline phosphatase and serum bilirubin, increased cephalin flocculation and thymol turbidity, and the like. Obviously, such patients require intensive nutritional rehabilitation along with the antabus program.

EVALUATION OF RESULTS

It is too early to appraise the long-term effects of antabus, but initial results in a series of approximately 30 patients give much basis for cautious optimism. To illustrate, several patients with 15 to 25 years of chronic alcoholism and numerous prior hospitalizations with only very transient benefit are maintaining sobriety with antabus and making an adequate social and occupational adjustment with the help of correlated therapies. Many of these patients probably will have to continue this "insurance policy" for a long time to come, just as the diabetic must often continue insulin daily. In the series here under review, the therapeutic results thus far with antabus and correlated therapy have been substantially favorable in approximately 80 per cent of cases.

It is necessary, however, to sound a note of caution. Antabus should be considered a two-edged sword, since the drug is potentially toxic and improperly used might be disastrous. A long-suffering wife, for instance, might put a few tablets into the coffee of her bibulous spouse. Hardly less dangerous would be indiscriminate prescription by physicians without adequate clinical and laboratory investigation beforehand. At present it would seem essential to limit use of the drug to properly staffed institutions, where, of course, both in-patient and out-patient treatment might be undertaken.

ANALYSIS OF THERAPEUTIC FAILURES

About 20 per cent of the patients in this series have not been able to maintain sobriety for a significant period. In each case, of course, the patient quit taking antabus. This points up one of the chief paradoxes in the problem of alcoholics—namely the strong (but largely unconscious) wish to fail or relapse coexisting with the often desperate, conscious desire to overcome the illness. Naturally, this same conflict is present in other psychiatric conditions but rarely to the intense degree found in the average problem drinker. This unconscious drive to disaster has been variously explained. Freud formulated an elaborate if not easily credible theory about a "death instinct." Karl Menninger has written extensively along these lines, referring especially to the "chronic suicide" of the alcoholic. Taking a somewhat different point of view, Bergler has emphasized the role of super-ego tension and the compulsion for self-punishment. From his own observations the author inclines toward the theory that the alcoholic constantly is unconsciously striving to recapture the infantile feeling of omnipotence. Closely related is his "chaos drive," or the need to smash everything to pieces, overwhelm and engulf his environment — much as the infant sends his blocks flying in all directions. The alcoholic is notorious for his inability to follow a regular program, especially one involving self-discipline. Under the pressure of responsibilities in the adult world he has strong drives to "kick over the traces" and smash everything up, including himself. This phenomenon seems to account for the apparent lack of capacity of some of the patients in this series to take a little white pill daily, even though failure to do so jeopardizes everything they consciously hold dear. To combat this aspect of the problem in this group of patients intensive deep-level psychotherapy, supplemented by special accessory techniques, seems to offer the best hope of amelioration. Of course, each time the alcoholic suffers a painful relapse, a certain amount of the reality principle may be driven home to him.

ILLUSTRATIVE CASES

CASE 1: A 54-year-old accountant was admitted to the Sierra Madre Lodge on December 28, 1949, in a heavily intoxicated condition. After detoxification with insulin, intravenous fluids, and endocrine support, thorough clinical evaluation revealed an underlying psychoneurotic tension state of severe degree along with moderate nutritional depletion. Life history revealed an overconscientious, obsessively worrisome and insecure person who had always overextended himself in his occupation to secure approval. Chronic gastrointestinal complaints of 35 years' standing seemed primarily related to a mixture of anxiety and suppressed resentment. Alcohol had been taken in progressively greater quantities during the past 20 years for sedation and escape, until a well-established secondary addiction had developed. The patient began to lose time from work, sporadically had a few days' treatment in "sobering up" sanitaria, and finally was dismissed from his job despite an otherwise excellent work record.

After proper study, this patient was started on antabus and correlated psychiatric therapy, in which sodium pentothal narcoanalysis was particularly effective. Within eight days after admission he had improved sufficiently to leave the hospital and continue on an out-patient basis. He has remained sober to date, takes antabus regularly, and claims no desire to drink. Perhaps more hopeful is the pronounced reduction in emotional tension and associated gastrointestinal disturbances. The patient secured a better job in a bank after the bank president convinced himself of the kind of rehabilitation this patient seems to have embarked on.

It is believed that for good long-term results, the patient will have to continue antabus for a minimum of two years, with periodic psychiatric interviews and occasional narcotherapy.

CASE 2: A 37-year-old professional man began the antabus program in September 1949. He was considered a primary addict of severe degree, having been a problem drinker since first touching alcohol at age 15. The history included several arrests for drunkenness and between 40 and 50 periods of hospitalization in a dozen sanitaria. No therapy seemed to have made any real impression, including office psychotherapy, the Alcoholics Anonymous program, emetine aversion therapy on four occasions, and the combined entreaties and exhortations of friends and relatives. Accordingly, the patient begged for antabus and reacted so thoroughly to the third alcohol reaction test that he acquired a very healthy fear of its effects, in contrast to the transient impression of emetine.

After graduating to out-patient status in one week, the patient did well for about the next three months. He was strongly urged to have comprehensive follow-up treatment, in the way of reeducative psychotherapy and nutritional correction. He cooperated at first but pleaded increasing difficulty in keeping appointments because of the pressure of business. A few days before Christmas the patient's wife reported he was drinking again. A few hours later the patient himself made an appeal to be readmitted to the sanitarium, averring that he was sicker than he had ever been in his life. After he had been rescued, he related that he had not taken antabus for seven days (missing the first two days "unconsciously" and the remainder intentionally) and had expected to "celebrate the holidays with a little drinking before returning to the program." However, he still retained enough antabus sensitization to cause profound reaction so that there was not even temporary enjoyment in drinking. Since that brief escapade the patient has had his business partner administer the prescribed medication to him daily and has remained entirely abstinent and regularly at work. To his friends and associates this sobriety borders on the miraculous, but to his physicians the basic emotional immaturity of the patient and the related tensions severely interfere with his functioning anywhere near his potential capacities. Later, when more receptive, this patient will require more psychiatric therapy, and in the meantime his "chaos drive" is apt to disrupt an already unstable equilibrium. On the other hand, each day that he remains sober on antabus is that much on the credit side of the ledger from many standpoints and should not be lightly dismissed.

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Discussion by NICHOLAS A. BERCEL, M.D., *Los Angeles*

Since the psyche is a public domain, the psychiatric specialist is confronted by laymen's opinions to a much greater degree than let us say a surgeon, whose province is not open to public inquiry. It is for this reason that psychiatrists had to take a considerable amount of public beating because even though they have hammered into the public mind monotonously that alcoholic patients need psychotherapy, their record of success, let us face it, was a poor one. Many psychiatrists went even as far as to surrender the alcoholic case material into the hands of laymen's organizations, which did not help in promoting public confidence in the efficacy of psychological treatment in general. Chief reason for this abyss existing between theory and practice is that the alcoholic patient is like a castle surrounded by a moat over which, up to recently, no bridge could carry us. The best conceived therapeutic program was of no avail as long as the patient was inaccessible, as long as we could not keep him sober between two visits.

The treatments based on antagonism or aversion to which antabus therapy has been added of late, perform the function of the bridge. Alcoholics are now within our reach. As the speaker so carefully emphasized, however, antabus is only one part in an integrated strategy of total push.

The available clinical evidence can be accepted with justifiable optimism. At first glance, the practice of relying on the alcoholic for taking his daily tablet seems to be a handicap. The temptation of not taking the tablet appears to be too great. On second analysis, however, the active part that the alcoholic patient has to take every day in his salvation program represents a daily renewed insurance policy, just as there are people who while unable to lay aside a fraction of their income *every month*, by putting pennies *every morning* in a "piggy bank" succeed in saving up a fortune.

Another advantage of antabus seems to lie in the fact that if an alcoholic is tempted to "beat" the untoward effect of antabus therapy by ingesting a whopping dose of alcohol he is likely to pass out before he has a chance to ponder over the success of his endeavor. Learning from bad experience is not necessarily a bad teacher. The most appealing feature of antabus therapy, however, is its psychological soundness and the opportunity that it offers to study the biochemistry of alcohol metabolism in the body.

I think the speaker deserves our congratulations for lifting our spirits and for the restraint with which he tried to keep this lift within bounds.